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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/552,591	08/02/2006	Menachem Rubinstein	RUBINSTEIN10A	1894

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EXAMINER	
KOSAR, ANDREW D	

ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
06/22/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/552,591	RUBINSTEIN ET AL.	
	Examiner	Art Unit	
	ANDREW D. KOSAR	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8 and 17-23* is/are pending in the application.

4a) Of the above claim(s) *17-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/6/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-8 and 17-23 are pending in the amendment filed October 6, 2005.

Election/Restrictions

Applicant's election with traverse of Group I in the reply filed on April 3, 2009 is acknowledged. The traversal is on the ground(s) that Applicant asserts the Fmoc derivatives of the prior art "have nothing to do with the common technical feature linking Groups I and II" and that the prior art used the Fmoc as a protecting group for synthesis, while here, it is asserted to be for the preparation of PYY analogs having prolonged half life. This is not found persuasive because the claims are drawn to products, and as indicated in the restriction, art capable of anticipating the independent product claim was discovered, thus the technical feature is not a contribution over the art.

The requirement is still deemed proper and is therefore made FINAL.

Claims 17-23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on April 3, 2009.

Priority & Oath

Applicant's claim of priority to US Provisional 60/460,820 is acknowledged. However, it is noted that Applicant has indicated on the oath that the claim is for the benefit of foreign priority. US provisional applications are not foreign priority documents. Appropriate is suggested to amend the claim to be a claim for the benefit under 35 USC 119(e).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over PITTNER (US 2002/0141985 A1; PTO-1449), PELLET (US Patent 6,217,893 B1), GERSHONOV (E. Gershonov et al. J. Med. Chem. (2000) 43(13), pages 2530-2537), SCHECHTER (Y. Schechter et al. Proc. Natl. Acad. Sci. (2001) 98(3), pages 1212-1217) and FRIDKIN (WO 98/05361 A2).

The instant claims are drawn generally to PYY agonists modified with Fmoc or FMS.

Pittner teaches PYY and PYY[3-36] and that the peptides are C-terminally amidated when expressed physiologically.

Pellet teaches sustained release compositions of proteins and peptides, including PYY. Pellet further teaches that, "The value of administering active principles in the form of sustained release compositions has been known for a long time, whether they be conventional pharmaceutical products, for example steroids, peptides or proteins, or products used in plant

protection." (column 1, lines 24-30). Thus, from the teachings of Pellet, it is understood in the art that peptide pharmaceuticals would benefit from sustained release pharmacokinetics.

Gershonov, Schechter and Fridkin each teach the advantages of using Fmoc and FMS to increase the circulating half-life. For example, Gershonov teaches that $(FMS)_3$-insulin "evades receptor-mediated endocytosis and degradation and, hence, persists for a long period in the circulation. The insulin consituent of the $(FMS)_3$-insulin conjugate undergoes a slow, spontaneous activation in the circulatory system, manifesting a prolonged glucose lowering action *in vivo*." (Abstract). Schechter teaches IFN-α2 derivative with FMS that, "is resistant to *in situ* inactivation and has the capability of slowly reverting to the native active protein at physiological conditions *in vivo* and *in vitro*." (Abstract). Schechter further teaches that "Protein drugs of molecular mass lower than 50,000 daltons are in general short-lived species *in vivo*, Having a circulatory half-life of about 5-20 min. Clearance of proteins occurs through several mechanisms, including glomerular infiltration in the kidney, receptor-mediated endocytosis and degradation by peripheral tissues and proteolysis at the tissue surfaces or by serum proteases. Considering also that protein drugs are not absorbed orally, prolonged maintenance of therapeutically active drugs in circulation is a desirable feature of primary clinical importance. Thus condition, however, is rarely achieved after a single administration of low molecular weight peptides and protein drugs." (page 1212). Schechter further teaches that they had "previously linked FMS moieties to the amino groups of several proteins" (page 1216) and that they found that "in aqueous neutral solutions, FMS moieties undergo slow, spontaneous hydrolysis with the generation of the native proteins." (page 1216). Fridkin teaches Fmoc and FMS have been used in the same manner to generate prodrugs (e.g. page 5, lines 22-28; abstract),

teaching that, "According to the novel concept of the present invention, numerous currently applied drugs can be converted into inactive prodrugs that are long-lived species as they evade general and receptor-mediated degradation in the organism. The prodrugs of the invention are designed to undergo spontaneous regeneration into the original drugs under *in vivo* physiological conditions and in a homogeneous fashion." (page 7, lines 3-7).

The difference between the instant claims and the teachings of the prior art, is that while the prior art teaches attachment of Fmoc/FMS to proteins/peptides, it does not teach attachment to PYY or PYY[3-36].

It would have been obvious to have made the Fmoc/FMS conjugate of PYY/PYY[3-36], in order to achieve the advantages of the increase half-life, evading of receptor-mediated endocytosis and degradation. One would have been motivated to have made the conjugates, as the prior art recognizes that PYY/PYY[3-36] would benefit from being a sustained release preparation, and modification with Fmoc/FMS would provide such benefit. Further, one would reasonably expect the FMS/Fmoc PYY/PYY[3-36] conjugates to have such properties, as Gershonov, Schechter and Fridkin each teach that such benefit is provided by the Fmoc/FMS moieties for any protein, and specifically exemplify the benefit for insulin and IFN-α2, and Schechter indicates that they had "previously linked FMS moieties to the amino groups of several proteins". With regards to the pharmaceutical compositions, PYY is a well known pharmaceutical peptide, and necessarily must be administered as part of a pharmaceutical composition, and thus the artisan would necessarily recognize that the conjugate would require being in a pharmaceutical composition for administration.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the foregoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANDREW D. KOSAR whose telephone number is (571)272-0913. The examiner can normally be reached on Monday - Friday 08:00 - 16:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia J. Tsang can be reached on (571)272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Andrew D Kosar/
Primary Examiner, Art Unit 1654